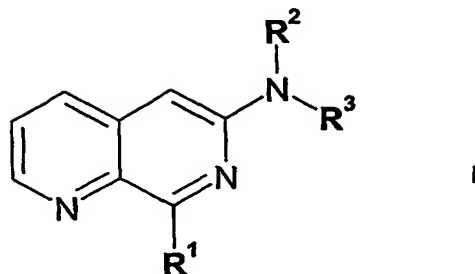


CLAIMS

1. A compound of formula I



in free or salt form, where

R¹ is a monovalent aromatic group having up to 10 carbon atoms, and

R² and R³ together with the nitrogen atom to which they are attached denote a heterocyclic group having up to 10 ring atoms and having 1 to 4 hetero atoms in the ring system.

2. A compound according to claim 1, in which

R¹ is phenyl substituted by one or two substituents selected from cyano, halogen, carboxy or C₁-C₄-haloalkoxy, and optionally by C₁-C₄-alkyl or C₁-C₄-alkoxy, or R¹ is phenyl substituted by C₁-C₄-alkoxy, and

R² and R³ together with the nitrogen atom to which they are attached denote a heterocyclic group having up to 6 ring atoms and one or two hetero atoms in the ring.

3. A compound according to claim 1, in which

R¹ is phenyl substituted by one or two substituents selected from cyano, halogen, carboxy or C₁-C₄-haloalkoxy meta to the indicated naphthyridine ring and optionally by C₁-C₄-alkyl or C₁-C₄-alkoxy ortho to the indicated naphthyridine ring, or R¹ is phenyl substituted by C₁-C₄-alkoxy meta to the indicated naphthyridine ring, and

R² and R³ together with the nitrogen atom to which they are attached denote a heterocyclyl group having up to 6 ring atoms and one or two nitrogen atoms, or one nitrogen atom and one oxygen atom, in the ring, optionally substituted by hydroxy, carboxy, 5-membered O-heterocyclylcarbonyl, aminocarbonyl, C₁-C₄-alkoxycarbonyl, C₁-C₄-alkylsulfonyl or C₁-C₄-alkyl optionally substituted by hydroxy, cyano, carboxy or C₁-C₄-alkoxycarbonyl.

4. A compound according to claim 1 in which

R<sup>1</sup> is phenyl optionally substituted by one, two or three substituents selected from the group consisting of cyano, C<sub>1</sub>-C<sub>8</sub>-alkyl, C<sub>1</sub>-C<sub>8</sub>-alkylthio, -SO-C<sub>1</sub>-C<sub>8</sub>-alkyl, and phenyl fused with a heterocyclic ring having 3 to 8 ring atoms of which up to 4 can be carbon atoms and up to 4 can be hetero atoms, and

R<sup>2</sup> and R<sup>3</sup> together with the nitrogen atom to which they are attached denote a heterocyclic group having up to 6 ring atoms and one or two hetero atoms in the ring optionally substituted by carboxy, carboxy-C<sub>1</sub>-C<sub>8</sub>-alkoxy or C<sub>1</sub>-C<sub>8</sub>-alkoxycarbonyl-C<sub>1</sub>-C<sub>8</sub>-alkoxy, said heterocyclic group also optionally being substituted by C<sub>1</sub>-C<sub>8</sub>-alkyl or C<sub>1</sub>-C<sub>8</sub>-alkoxy.

5. A compound according to claim 4, in which

R<sup>1</sup> is phenyl optionally substituted by one, two or three substituents selected from the group consisting of cyano, C<sub>1</sub>-C<sub>4</sub>-alkyl, C<sub>1</sub>-C<sub>4</sub>-alkylthio, -SO-C<sub>1</sub>-C<sub>4</sub>-alkyl, and phenyl fused with a heterocyclic ring having 5 or 6 ring atoms of which up to 4 can be carbon atoms and up to 2 can be hetero atoms, and

R<sup>2</sup> and R<sup>3</sup> together with the nitrogen atom to which they are attached denote a heterocyclic group having up to 6 ring atoms and one or two nitrogen atoms in the ring optionally substituted by carboxy, carboxy-C<sub>1</sub>-C<sub>4</sub>-alkoxy or C<sub>1</sub>-C<sub>4</sub>-alkoxycarbonyl-C<sub>1</sub>-C<sub>4</sub>-alkoxy, said heterocyclic group also optionally being substituted by C<sub>1</sub>-C<sub>4</sub>-alkyl.

6. A compound according to claim 1, which is

3-[6-(3-hydroxy-pyrrolidin-1-yl)-[1,7]naphthyridin-8-yl]-benzonitrile;

3-[6-[4-(2-cyano-ethyl)-piperazin-1-yl]-[1,7]naphthyridin-8-yl]-benzonitrile;

1-[8-(3-cyano-phenyl)-[1,7]naphthyridin-6-yl]-piperidine-4-carboxylic acid, lithium salt; or

3-(6-piperazin-1-yl-[1,7]naphthyridin-8-yl)-benzonitrile;

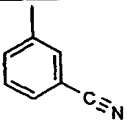
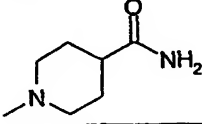
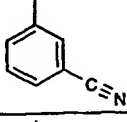
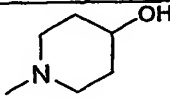
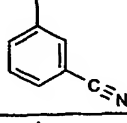
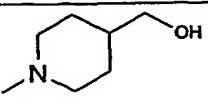
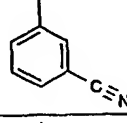
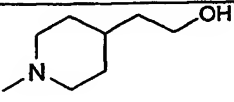
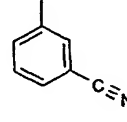
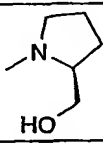
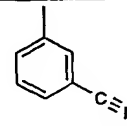
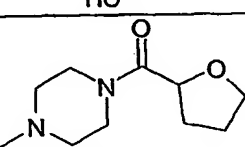
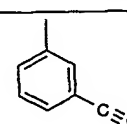
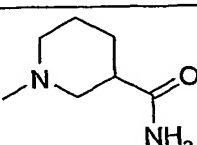
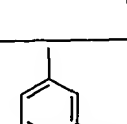
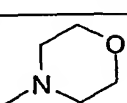
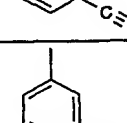
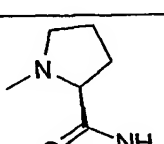
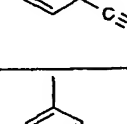
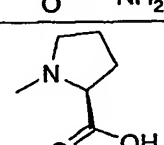
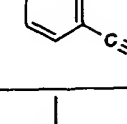
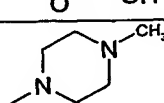
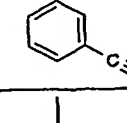
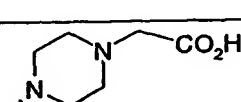
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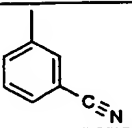
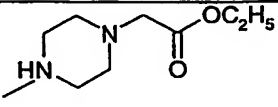
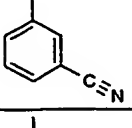
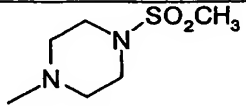
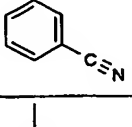
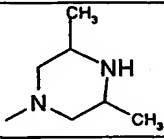
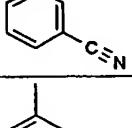
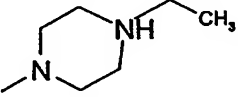
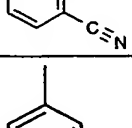
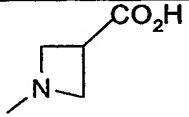
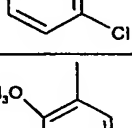
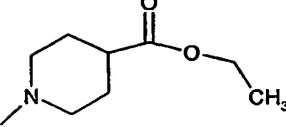
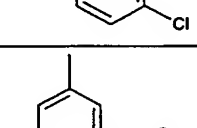
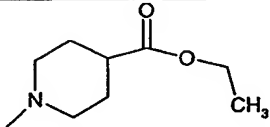
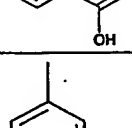
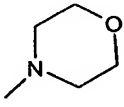
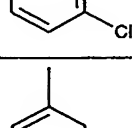
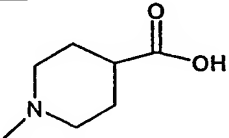
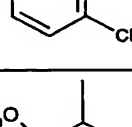
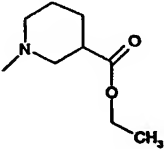
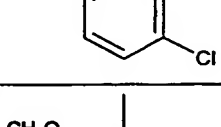
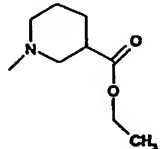
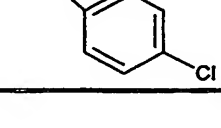
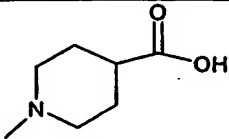
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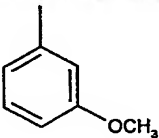
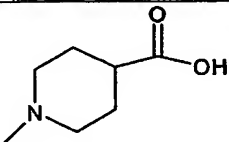
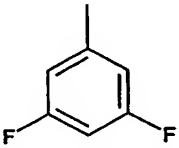
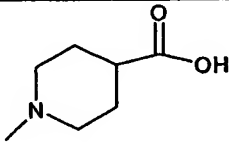
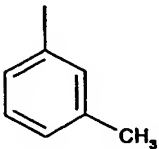
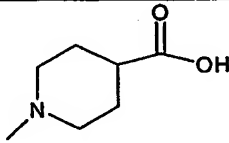
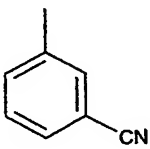
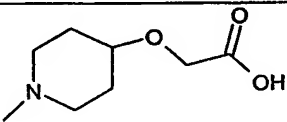
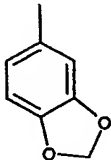
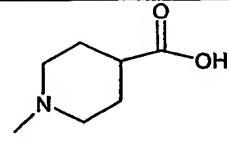
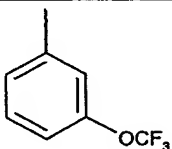
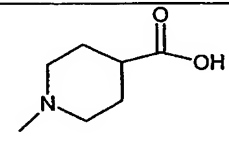
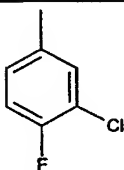
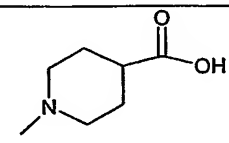
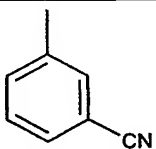
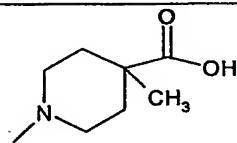
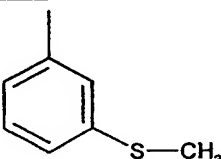
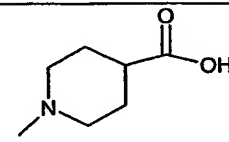
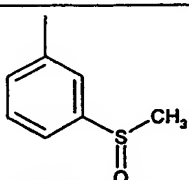
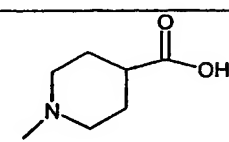
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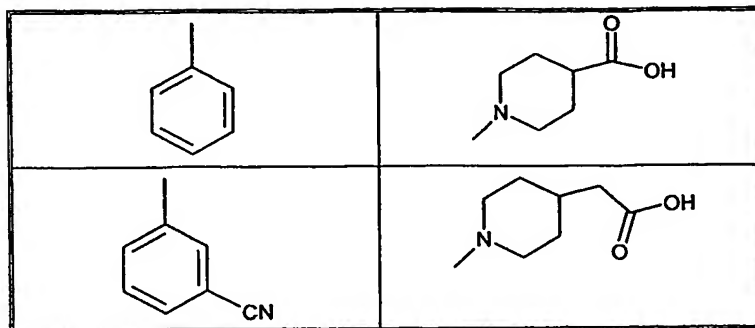
potassium 1-[8-(5-fluoro-2-methoxy-phenyl)-[1,7]naphthyridin-6-yl]-piperidine-4-carboxylate.

7. A compound according to claim 1, wherein R<sup>1</sup> and -NR<sup>2</sup>R<sup>3</sup> are as shown in the following table:

$R^1$	$NR^2R^3$
	
	
	
	
	
	
	
	
	
	
	
	

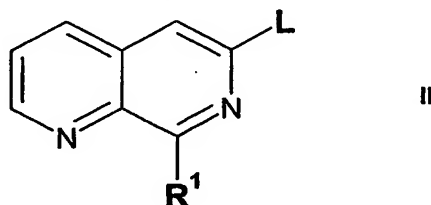
	
	
	
	
	
	
	
	
	
	
	
	

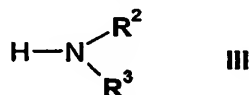


8. A compound according to any one of the preceding claims for use as a pharmaceutical.
9. A pharmaceutical composition comprising a compound according to any one of claims 1 to 7, optionally together with a pharmaceutically acceptable diluent or carrier.
9. Use of a compound according to any one of claims 1 to 7 for the preparation of a medicament for the treatment of a condition mediated by PDE4.
10. Use of a compound according to any one of claims 1 to 7 for the preparation of a medicament for the down-regulation or inhibition of TNF- $\alpha$  release.
11. Use of a compound according to any one of claims 1 to 7 for the preparation of a medicament for the treatment of an inflammatory disease.
12. Use of a compound according to any one of claims 1 to 7 for the preparation of a medicament for the treatment of an obstructive or inflammatory airways disease.
13. A process for the preparation of compounds of formula I in free or salt form which comprises

(iii) (A) reacting a compound of formula



optionally in protected form, where  $R^1$  is as hereinbefore defined and L is a leaving atom or group, for example halogen or an aliphatic or aromatic sulfonyloxy group such as trifluoromethylsulfonyloxy, with a compound of formula



optionally in protected form, where  $R^2$  and  $R^3$  are as hereinbefore defined, followed by deprotection if required;

(B) reacting a compound of formula I, where  $R^2$  and  $R^3$  together with the attached nitrogen atom denote a heterocyclyl group substituted by a  $C_1$ - $C_8$ -alkoxycarbonyl group, to convert the alkoxycarbonyl group into a carboxy;

(C) for the preparation of compounds of formula I where  $R^2$  and  $R^3$  together with the attached nitrogen atom denote a heterocyclyl group substituted by carboxy- $C_1$ - $C_8$ -alkoxy, hydrolysing a compound of formula I where  $R^2$  and  $R^3$  together with the attached nitrogen atom denote a heterocyclyl group substituted by  $C_1$ - $C_8$ -alkoxycarbonyl- $C_1$ - $C_8$ -alkoxy; or

(D) for the preparation of compounds of formula I when  $R^1$  is phenyl substituted by -SO- $C_1$ - $C_8$ -alkyl, oxidising a compound of formula I where  $R^1$  is phenyl substituted by  $C_1$ - $C_8$ -alkylthio; and

(iv) recovering the product in free or salt form.